Lung Cancer 126 (2018) 41–47

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

A phase II study of afatinib treatment for elderly patients with previously untreated advanced non-small-cell lung cancer harboring *EGFR* mutations

Hisao Imai[a], Kyoichi Kaira[b,*], Kensuke Suzuki[c], Masaki Anzai[d], Takeshi Tsuda[c], Tamotsu Ishizuka[d], Tomohito Kuwako[e], Ichiro Naruse[f], Kenji Nemoto[g], Junji Uchino[h], Nobutoshi Morozumi[i], Shinichi Ishihara[j], Koichi Minato[a], Takeshi Hisada[k]

[a] *Division of Respiratory Medicine, Gunma Prefectural Cancer Center, Ohta, Gunma, Japan*
[b] *Department of Oncology Clinical Development, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan*
[c] *Division of Internal Medicine, Toyama Prefectural Central Hospital, Toyama, Toyama, Japan*
[d] *Third Department of Internal Medicine, Faculty of Medical Sciences, University of Fukui, Eiheiji, Fukui, Japan*
[e] *Division of Respirology, National Hospital Organization Shibukawa Medical Center Hospital, Shibukawa, Gunma, Japan*
[f] *Division of Respiratory Medicine, Hidaka Hospital, Takasaki, Gunma, Japan*
[g] *Division of Respiratory Medicine, National Hospital Organization Ibarakihigashi National Hospital, Tokai, Ibaraki, Japan*
[h] *Department of Pulmonary Medicine, Kyoto Prefectural University of Medicine, Kyoto, Kyoto, Japan*
[i] *Division of Respiratory Medicine, Saku Central Hospital Advanced Care Center, Saku, Nagano, Japan*
[j] *Division of Internal Medicine, Isesaki Municipal Hospital, Isesaki, Gunma, Japan*
[k] *Department of Respiratory Medicine, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan*

Elderly patients for afatinib

非小細胞肺癌患者

化学療法未治療の非小細胞肺癌患者（１次治療）
・EGFR遺伝子変異　陽性
exon 19 deletion
exon21 L858R
(T790M exclude)

afatinib
n=40
30mg/day
Up to PD

ORR	DCR	mPFS
72.5%	100%	12.9ヶ月

Hisao Imai[a], Kyoichi Kaira[b,], Lung Cancer2018

(EGFR-TKI-116)

A B S T R A C T

Objective: The efficacy and safety of afatinib in elderly patients with *EGFR*-mutated non-small-cell lung cancer (NSCLC) have not been evaluated. This study aimed to assess the efficacy and safety of afatinib in elderly chemotherapy-naive patients with NSCLC harboring sensitive *EGFR* mutations.

Materials and Methods: We prospectively assessed the clinical effects of afatinib as a first-line treatment for elderly (age ≥70 years) NSCLC patients with *EGFR* mutations (exon 19 deletion or exon 21 L858R mutation). All patients were initially administered afatinib (30 mg/day).

Results: Between May 2014 and August 2017, 40 patients (13 men, 27 women) with adenocarcinoma were included in our analysis. The median age was 77 years (range, 70–85 years). The dose was reduced in 19 patients. The objective overall response and disease control rates were 72.5% and 100%, respectively, and the median progression-free survival and overall survival were 12.9 months and not reached, respectively. Common adverse events (AEs) included diarrhea, rash/acne, and anemia. Major grade 3 or higher toxicities included diarrhea (12.5%), mucositis (7.5%), and pneumonitis (7.5%). Afatinib treatment was discontinued in 8 patients owing to AEs of elevated amylase (n = 1), liver dysfunction (n = 1), rash/acne (n = 1), nail change (n = 1), anorexia (n = 2), pneumonitis (n = 2), and diarrhea (n = 2). Two patients died due to treatment-related pneumonitis.

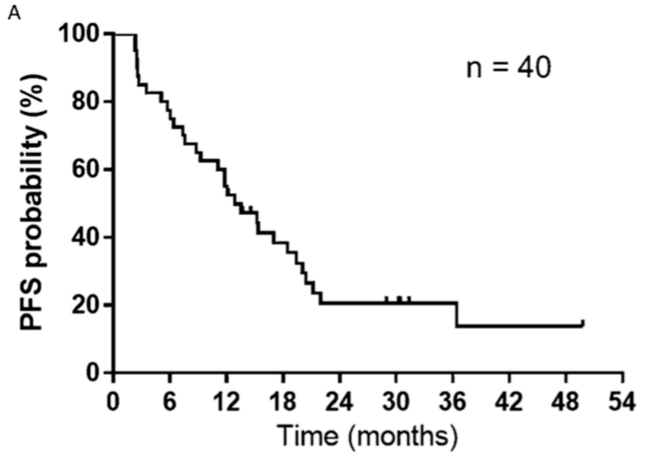
Conclusions: This is the first study that verified the efficacy and feasibility of first-line chemotherapy with afatinib at 30 mg/day in elderly patients with advanced NSCLC harboring sensitive *EGFR* mutations. First-line afatinib of 30 mg/day could be a treatment option in this patient population.

Table 1
Patients Characteristics.

?→Characteristics	N = 40	(%)
Sex		
Women	27	67.5
Men	13	32.5
Age		
Median	77	
Range	70-85	
Smoking status		
Never	31	77.5
Former	9	22.5
Current	0	0
Performance status		
0	18	45
1	21	52.5
2	1	2.5
Stage		
IIIB	0	0
IV	34	85
Postoperative recurrence	6	15
Histology		
Adenocarcinoma	40	100
EGFR mutation type		
ex19 deletion	22	55
ex21 L858R	18	45
Comorbidity		
Hypertention	12	30
Diabetes Mellitus	4	10
Arrythmia	3	7.5
COPD	1	2.5
Dose reduction (30 mg→20 mg)		
Yes	19	47.5
No	21	52.5

Table 2
Response Rate of Treatment With Afatinib.

Response	N = 40	(%)
CR	1	2.5
PR	28	70
SD	11	27.5
PD	0	0
Response rate (%)		72.5
Disease control rate[a] (%)		100



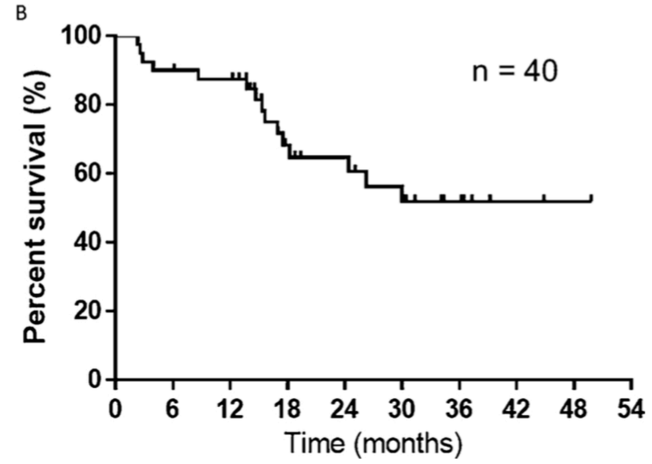


Table 3
Safety—Nonhematologic and Hematologic or Laboratory Adverse Events.

	NCI-CTCAE Grade (Ver 3.0)					
Event	1	2	3	4	5	≥3 (%)
Nonhematologic adverse events						
Fatigue	5	2	0	0	–	0 (0)
Dry skin	8	5	1	–	–	1 (2.5)
Nail changes	6	7	2	–	–	2 (5.0)
Pruritus	6	1	0	–	–	0 (0)
Rash/acne	15	11	2	0	0	2 (5.0)
Urticaria	4	1	0	–	–	0 (0)
Anorexia	5	9	2	0	0	2 (5.0)
Diarrhea	19	7	5	0	0	5 (12.5)
Mucositis	9	5	3	0	0	3 (7.5)
Nausea	1	2	1	0	0	1 (2.5)
Vomiting	0	2	0	0	0	0 (0)
Infection	–	1	1	0	0	1 (2.5)
Pneumonitis	1	0	1	0	2	3 (7.5)
Hematologic or laboratory adverse events						
Hemoglobin	20	4	0	0	0	0 (0)
ALT	4	1	2	0	–	2 (5.0)
AST	1	1	2	0	–	2 (5.0)
Bilirubin	1	1	0	0	–	0 (0)
Amylase	0	0	0	1	–	1 (2.5)

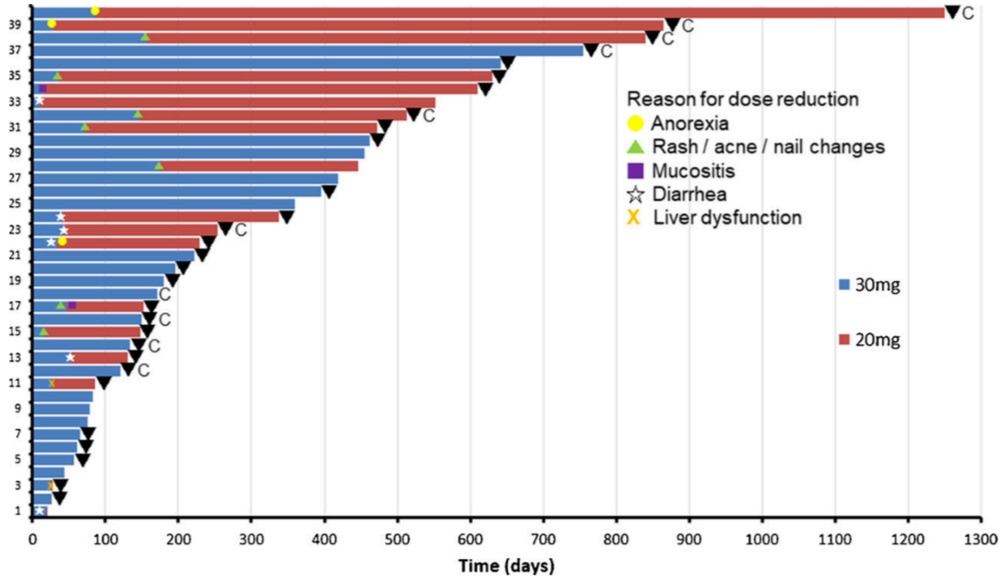


Fig. 2. Treatment duration and afatinib dosage in the overall population. ▼: case of CR or PR; C: continuing protocol treatment.

Table 4
A summary of reports regarding EGFR-TKI treatments in elderly patients with epidermal growth factor receptor-mutated non-small cell lung cancer.

Author	Drug	No. of Pts	Study design	Sex (male/female)	ECOG PS (0/1/2/3/4)	Histology (Ad/Sq/Other)	Smoking history (Yes/No)	*EGFR* mutation type (ex19del/ex21 L858R/other)	Age (years)	Median age (range)	Response rate (%)	Median PFS (months)	Median OS (months)
Maemondo et al. [13]	GEF	31	Prospective	25/6	16/13/2/0/0	30/0/1	8/23	NR	≥75	80.3 (75–89)	74	12.3	33.8
Fujita et al. [14]	GEF	22	Prospective	5/17	8/14/0/0/0	21/1/0	6/16	6/14/2	≥70	81 (71–85)	45.5	9.7	27.9
Takahashi et al. [15]	GEF	20	Prospective	7/13	13/5/2/0/0	20/0/0	6/14	12/8/0	≥70	79.5 (72–90)	70	10	26.4
Uruga et al. [16]	GEF	9	Retrospective	1/8	4/3/1/1/0	9/0/0	0/9	5/3/1	≥70	79 (73–89)	66.7	13.1	17.2
Tateishi et al. [17]	GEF	55	Retrospective	16/39	21/25/0/0/0	55/0/0	16/39	31/24/0	≥75	81.1 (75–94)	72.7	13.8	29.1
Kuwako et al. [18]	GEF	62	Retrospective	17/45	17/27/7/10/1	61/0/1	15/47	24/38/0	≥75	80 (75–89)	61.3	13.2	19
Morikawa et al. [19]	GEF	71	Retrospective (pooled analysis)	19/52	34/31/6/0/0	64/0/4	18/53	35/32/4	≥70	75 (70–89)	73.2	14.3	30.8
Inoue et al. [21]	ERL	32	Prospective	9/23	22/9/1/0/0	32/0/0	9/23	12/20/0	≥75	80 (75–87)	56.3	15.5	Not reached
Wu et al. [32]	AFA	19	Prospective (subgroup analysis)	5/14	3/16/0/0/0	19/0/0	6/13	7/12/0	≥75	79 (75–86)	NR	14.7	27.9
Current report	AFA	40	Prospective	13/27	18/21/1/0/0	40/0/0	9/31	22/18/0	≥70	77 (70-85)	72.5	12.9	Not reached

Pts, patients; ECOG PS, Eastern Cooperative Oncology Group performance status; Ad, adenocarcinoma; Sq, squamous cell carcinoma; EGFR, epidermal growth factor receptor; PFS, progression-free survival; OS, overall survival; NR, not reported; GEF, gefitinib; ERL, erlotinib; AFA, afatinib.